REMARKS

CLAIM STATUS AND AMENDMENTS

The Office Action states that the amendment dated March 10, 2008 was not entered. Claims 26-46, which were presented in the Preliminary Amendment dated May 15, 2006, are therefore currently pending and subject to a restriction requirement.

The Office Action also states that claims 26-45 are pending and subject to restriction. To clarify, claims 26-46 are pending.

Claims 26-46 are now canceled and new claims 47-67 are added. Claims 47-67 correspond respectively to previous claims 26-46 but have been drafted to further clarify the intended subject matter, correct typographical errors, provide proper antecedent basis, and better conform to U.S. patent practice.

The specification has been amended to provide appropriate SEQ ID NOs and to replace the Sequence Listing of record.

Support for the amendments can be found in the specification and original claims as filed. No new matter has been added.

COMPLIANCE WITH SEQUENCE RULES

The Office Action states that previous claims 26-46 do not comply with the sequence rules. In response, Applicants amend

the specification and claims, and submit a replacement Sequence Listing. The amendments respond to the sequence rule issues noted in the present Office Action, and also respond to the Notification to Comply dated January 16, 2008.

The foregoing amendments place the application in compliance with the Sequence Rules under 37 C.F.R. § 1.821-1.825.

The Sequence Listing is submitted in both paper and computer readable form (CRF) as required by 37 C.F.R. § 1.821(c) and (e). The Sequence Listing includes sequence identifiers that correspond to the peptide sequences in the disclosure. The Sequence Listing also includes the current application information per U.S. practice. The specification has been amended to insert the attached paper copy and CRF of the Sequence Listing and/or to replace the Sequence Listing of record. Support for such can be found in the originally filed application. No new matter has been added. Accordingly, the submission complies with 37 C.F.R. § 1.821(g).

The content of the paper and computer readable copies of the Sequence Listing are the same, and thus this submission complies with 37 C.F.R. § 1.821(c) and (e).

The attached Sequence Listing was run through the USPTO Checker software (Version 4.4.0) (October 25, 2005) and no errors were found.

In view of the foregoing, it is believed that each requirement set forth in the Office Action and the Notice to

Comply has been satisfied, and that the application complies with the Sequence Rules under 37 C.F.R. §§ 1.821-1.825.

RESTRICTION REQUIREMENT

In response to the restriction requirements, Applicants provisionally elect, with traverse, Group I, claims 26-31 and 35-45 (new claims 47-52 and 56-67) drawn to dual chain avidin (dcAvd) molecules, circularly permuted avidin monomers, DNA encoding such avidin molecules, and a method of expressing said DNA.

In further response to the restriction requirements, Applicants provisionally elect, with traverse, Group (h), drawn to cpAvd 5→4/cpAvd 6→5 fusions.

The instant application is a 371 National stage application of PCT/FI2004/000679. Thus, PCT rules regarding unity of invention apply under these circumstances.

PCT Rule 13.1 deals with the requirement of unity of invention and states that an international application should relate to only one invention, or if there is more than one invention, that the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept.

PCT Rule 13.2 defines the method for determining whether the requirement of unity of invention is satisfied in respect to a group of inventions claimed in an international

application. Unity of invention exists when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features." The expression "special technical features" is defined in Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.

The Office Action fails to satisfy the requirements of PCT Rule 13.1 and PCT Rule 13.2.

The Office Action asserts that the claims of Group I and Group II differ in structure and function and therefore do not share any technical feature. Applicants disagree with this position.

The present claims relate to dual-chain avidin (dcAvd) comprising the fusion of two avidin monomers. More specifically, the avidin monomers are circularly permuted wherein the natural termini (C-terminal and N-terminal) are joined and the monomer is opened at another point to create new C- and N- termini. The circularly permuted avidin monomers are fused and the resulting fusion proteins (dcAvd) can form a pseudo-tetrameric dual-chain avidin that maintains its biotin binding properties. (See, page 5, lines 5-17, of the specification).

As pointed out in the Office Action, the present claims feature monomers of wild-type avidin, mutant avidin, poultry avidin, streptavidin, and chicken avidin-related protein (AVR).

Granted, there can be diversity among these monomers at the primary structure (i.e., amino acid sequence) level, but more importantly, the diversity disappears at the secondary, tertiary and quarternary levels. Avidin is a homotetrameric protein, and each of the four avidin subunits is arranged in an eight-stranded antiparallel β-barrel, whose inner region defines the biotin binding site. Thus, although avidin and streptavidin share only about 30% amino acid sequence identity, avidin and streptavidin display an essentially identical structural and functional relationship. Avidin and AVR proteins are about 80% identical in amino acid sequence, but share the eight essential β-structures and almost all of the residues involved in biotin binding are conserved. Finally, the mutant and poultry avidin are even more closely similar to wild-type avidin.

Thus, all of the avidin monomers disclosed in the specification, and featured in new claims 47-67, are very much structurally related. The monomers all share the eight conserved β structures that define the biotin binding site. The β structures are also a featured part of the present claims.

As detailed in the specification, the dcAvd structures are formed from circularly permuted avidin that retains its native biological activity. Therefore, (1) the natural termini are joined in a manner such that creation of the linkage does not destroy biological activity, and (2) an “opening site” is picked that does not disrupt a region critical for protein folding and

desired biological activity. (See, page 11, lines 3-9). Regardless of which avidin monomers are utilized, and despite any variation in their primary structure or amino acid sequences, the dcAvd structures all maintain the same structural features at the secondary, tertiary and quarternary levels.

Regardless of whether the avidin monomer is wild-type, mutant, poultry, streptavidin, or chicken AVR, each of the monomers can form a circularly permuted avidin monomer defined by cpAvd5→4, cpAvd6→5 and cpAvd4→3 in claim 47, and each of the circularly permuted avidin monomers would retain biotin binding activity. This defines at least one technical relationship between the claims of Groups I and II, and each of the compounds of subgroups (a)-(j).

The claimed subject matter therefore clearly possesses unity of invention under PCT Rule 13.2. Therefore, Applicants respectfully request withdrawal of the lack of unity determination and a favorable action on the merits of the claims in their full scope.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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